PATENT SPECIFICATION

DRAWINGS ATTACHED

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COMPLETE SPECIFICATION

Means for Administering Drugs

I, HIGHAM STANLEY RUSSELL, a British Subject of 29 Camberley Drive, Rochdale, Lancashire, do hereby declare the invention, for which I pray that a patent may be granted to me, and the method by which it is to be performed, to be particularly described in and by the following statement:—

This invention concerns a vehicle for administering drugs.

It is well known that various drugs, be they hormonal preparations or otherwise, are destroyed or inactivated by saliva in the mouth or fluids in the stomach if they are administered by way of the digestive tract, and certain drugs may have undesirable side effects when administered orally. Therefore, such drugs are, where possible, injected into the body, but this procedure is not very convenient to adopt in many circumstances, there being well known risks in the giving of injections.

Other drugs capable of being administered orally are only very slightly absorbed into the body through the stomach. In these cases, massive overdoses have to be administered, and this, too, is not very satisfactory as the rate of absorption varies considerably from patient to patient and accurate forecast of optimum dosage cannot be made.

In certain instances drugs should desirably be administered gradually and progressively only until a desired effect is obtained, and this is difficult to carry out with the means hitherto available.

An object of the invention is to provide a vehicle for administering drugs whereby the aforementioned difficulties are minimised, the vehicle providing for a particularly convenient, simple and accurate method of administration.

According to the present invention there is provided a vehicle for administering drugs, comprising an elongate strip of resiliently flexible gelatinous material of a cross-section which enables a length thereof conveniently to be inserted in the buccal sulcus so as to adhere to the gum thereat, the vehicle containing a drug (preferably of a type which, if swallowed, would be destroyed or inactivated by saliva or fluids in the stomach, or would produce undesired side effects, or would require to be administered in massive overdoses) which is effective when absorbed through the buccal mucous membrane of a person, the said strip being marked or otherwise formed at intervals therealong to facilitate it being divided up to provide individual lengths or sections of desired drug content or dosage.

The invention also provides a method of making a vehicle as aforesaid comprising the steps of preparing a liquid solution or melt of a gelatinous material, impregnating the solution or melt with the said drug and forming the impregnated solution or melt into the vehicle by moulding or extrusion.

The vehicle is preferably of a form of glycogelatine which is sufficiently firm and solid to be resilient, and is conveniently in the form of an extrusion of rectangular or oval cross section.

The invention will be described further, by way of example, with reference to the accompanying drawings, in which:—

Fig. 1 is an enlarged perspective view showing part of a first embodiment of the vehicle of the invention;

Fig. 2 is a section corresponding to the line II—II of Fig. 1;

Figs. 3, 4, 5, 6 and 7 are views similar to Fig. 2 but showing five suitable alternative cross-sections for the vehicle;

Figs. 8 and 9 are views similar to Fig. 1 but showing two further embodiments of the vehicle;

Fig. 10 is a diagrammatic view showing a small length of the vehicle of Figs. 1 and 2 in its position of use; and

Fig. 11 is a view similar to Fig. 10 but showing a longer length of the vehicle in use.

Referring firstly to Figs. 1 and 2, a vehicle for administering drugs in conformity with the invention comprises an elongate strip 10, generally of rectangular cross-section and made of a resilient flexible gelatinous material such as glyco-gelatine. Contained in such material is a drug the nature of which will be discussed later. As can be seen, the strip 10 is formed at intervals therealong with pairs of transverse depressions 11 in opposite major faces thereof so as to divide the strip into a plurality of sections 12 which are each connected to the next adjacent sections by comparatively weak ligaments 13.

The purpose of these ligaments 13 is to enable the strip 10 to be torn or otherwise divided up into individual lengths each of which consists of one or a desired number of the sections 12.

Fig. 10 shows how the vehicle of Figs. 1 and 2 may be used. A single section 12, after having been severed from the strip 10, is inserted into the buccal sulcus 14 at the front of a patient's mouth and is pressed firmly against the gum 15 thereat. Because the material of the section 12 is flexible and resilient and the gum is usually slightly moist with saliva, the section 12 can be pressed to the gum 15 so that it substantially immediately adheres to the gum 15 at the upper part thereof, to occupy substantially wholly the upper part of the space between the gum 15 and the adjacent lip 16. As soon as it adheres in position, the section 12 immediately excludes saliva from that part of the gum 15 which it overlies, and access thereto of saliva from the rest of the mouth is minimised by the lip 16. At the face of the material abutting the gum 15, such material slowly goes into solution and is absorbed into the patient's bloodstream through the gum 15, gradual dissolution of the material ensuring that there is a constant supply thereof available for absorption.

Assuming the vehicle 10 to have been produced so that each section 12 thereof contains a predetermined quantity of the drug, it will be evident that a desired dosage of the drug can be administered by the use of an appropriate number of the sections 12. Thus, whilst Fig. 10 shows a single section 12 in position for administration, a plurality thereof can be administered simultaneously as shown in Fig. 11, each of the sections 12 adhering to the gum 15 for absorption therethrough.

The vehicle 10 can be of any cross-section which is suitable for insertion into the buccal sulcus at the front of the user's mouth and which will readily adhere to the gum thereat. Thus, it may be square in cross-section as is the case of the vehicle 10*a* of Fig. 3, it may be circular (vehicle 10*b* of Fig. 4), oval (vehicle 10*c* of Fig. 5), of thin strip form with its two major faces 17 and 18 respectively convex and concave (vehicle 10*d* of Fig. 6) or of thicker strip form with convex and concave faces 19 and 20 respectively (vehicle 10*e* of Fig. 7). When sections 12 of the latter two vehicles 10*d* and 10*e* are used, the concave surfaces 18, 20 are pressed against the gum 15.

In the case of the two vehicles 10*d* and 10*e* of Figs. 6 and 7, the ligaments 13 are shown as having been defined by pairs of depressions 11 extending inwards from the opposite edges of the vehicle instead of from the opposite major faces 17, 18 and 19, 20. Naturally, it will be understood that these vehicles can be formed with depressions 11 similar to those of Figs. 1 to 5 and conversely the vehicles of Figs. 1 to 5 may have depressions similar to those of Figs. 6 and 7. A vehicle 10*f* comparable to those of Figs. 6 and 7 is shown in Fig. 8, the vehicle here being of substantially flat strip form to provide flat sections 12.

In all the forms of the vehicle so far described and illustrated, pairs of depressions 11 are provided at intervals along the strip, but it will be appreciated that the strip can equally well be divided or graduated into sections, preferably of equal sizes, by single depressions at intervals along the strip such depressions extending from edge to edge or from side to side of the strip, whereby the strip may readily be torn across, or extending only part of the way across the strip simply by way of graduations defining the individual sections 12 and providing appropriate indications for cutting the strip as desired, e.g. by use of scissors. Conversely, the strip can be marked or graduated by means of thickened ribs instead of depressions. Such a vehicle is illustrated at 10*g* in Fig. 9 wherein the vehicle is graduated in sections 12 by ribs 21 extending from edge to edge of the strip on one face only thereof. These ribs 21 can, of course, extend only part of the way across the strip.

The vehicles as described can be made in any suitable manner whereby glyco-gelatine may be formed into strips, and the following exemplifies one way in which it may be carried out.

Firstly the desired drug is stirred, mixed or otherwise thoroughly dispersed into a batch of glyco-gelatine solution or melt, and such material is then run into a series of moulds each of which is shaped according to the desired strip form of the vehicle, the glyco-gelatine, with the drug contained therein, being hardened and dried whilst in the moulds to such a degree that the strips, upon being stripped from the moulds can conveniently be handled yet are resilient and flexible.

Alternatively, the material containing the drug may be appropriately extended in con-

tinuous strip form, the graduations, depressions, ribs or other markings being subsequently produced thereon, for example by passing the strip through a nip formed by a pair of heated rollers shaped to form the depressions thereon.

The following is an example of a suitable composition for the gelatinous material:—

Gelatine B.P. — 45.48% by weight
Glycerine B.P. — 16.20% by weight
Water — 38.32% by weight

Small amounts of a preservative e.g. beta-naphthol, and the hormone or drug are added to the solution or melt, and then excess water is removed by drying, e.g. in the case of thermolabile medicaments, under reduced pressure, until the gelatinous material is resiliently flexible, and has the dissolution time required. The factors governing the rate of dissolution, and hence the rate of absorption of a given vehicle may be controlled by adjusting the composition of the melt. In general, the rate of absorption depends directly upon the proportions of water and glycerine present in the melt.

Other glyco-gelatine based mixtures, or a gelatinous material based on the alginates, or other suitable (e.g. resin-based) material may be used, but a material based on glyco-gelatine is preferred. The material of the above described Example will have a melting point near blood heat e.g. between 105° and 90°F. and is soft and resiliently pliable at the temperature usual in the mouth. Furthermore, the material is virtually non-toxic and has no side effects on the patient; it is soluble in water, is almost tasteless, and is thus suitable for absorption through the mucous membrane of the gum, i.e. in the buccal sulcus. These properties or proportion similar thereto are necessary for any alternative material.

The drug incorporated in the vehicle of the invention will be present in a small quantity e.g. a few microgrammes or milligrammes of the drug per centimetre length of the vehicle. The drug may be of various types such as those which are usually injected or given rectally because they are:—

(a) substantially destroyed or inactivated in the stomach or intestines, when ingested;
(b) active in an unwanted manner upon the stomach or intestines to produce undesirable side effects when ingested;
(c) variable in absorption or effect from patient to patient;
(d) slow to act when ingested so that they require massive overdoses to be effective; or
(e) of local application.

The principal types of drugs are as follows:—

Type 1

Hormones; their derivatives and analogues, such as the steroid hormones; and the polypeptide hormones e.g. vasopressin and insulin. Further examples are: testosterone; oestrogens, and progesterones.

Type 2

Local anaesthetics e.g., lignocaine hydrochloride and diperodon hydrochloride.

Type 3

Sympathomimetic amines e.g., adrenaline, noradrenaline, isoprenaline and amphetamine, and substances which have an opposing action such as ergotamine and dibenyline (Registered Trade Mark).

Type 4

Substances to be given when a prompt response may be desirable, e.g. vaso-dilators; quick acting diuretics; analgesics e.g. morphine; and cardiovascular reactants e.g. glyceryl trinitrate.

Type 5

Substances in relation to which it is not readily possible to determine the specific dose which should be administered to a particular patient, e.g. oxytocin, digitalin, barbiturates, muscle relaxants and ganglion blocking agents.

Type 6

Substances acting on the parasympathetic system, e.g. acetylcholine, anticholinesterases and physostigmine.

Type 7

Various other substances which are potent when absorbed, such as antihistamines, e.g. promethazine; alkaloids, and glycosides such as atropine and hyoscine; nitrates e.g. amyl nitrate; analeptics e.g. caffeine; cyto-toxic agents; anticoagulants e.g. heparin; vitamins such as cyanocobalamin; and trace element substances.

Type 8

Metabolic reactants for clinical investigations e.g. para-amino-hippuric acid.

It is possible to use any drug which is sufficiently stable, potent, and absorbable. A good example is insulin even though it has a substantial molecular weight.

In use when it is desired to administer a given amount of the drug, an appropriate length of the vehicle is severed from the strip and the severed length is inserted into the buccal sulcus as described. It is thereafter entirely absorbed into the gum or is allowed to be absorbed until the desired effect is obtained.

Due to the fact that the vehicle is, effectively, a solution of the drug in a gelatinous material, the rate of absorption is remarkably constant, especially when compared with the absorption rates of a tablet of compressed

particulate material having a similar overall concentration of the drug, but having a particulate character.

Furthermore, the vehicle does not fragment and therefore may be easily removed when sufficient of the drug has been absorbed, and the cut length will be readily retained in the sulcus due to its semi-plastic nature. Since the severed length of the vehicle is entirely contained within the buccal sulcus little or none of the drug need be washed away or inactivated by saliva, and since the vehicle is hardly felt when in place it does not provoke salivation. Furthermore, the vehicle is located away from the flow path of any saliva which may be secreted.

The length of the vehicle, being severed from a strip, may be chosen so as to facilitate the administration of an exact and chosen amount of the drug.

Due to its adhesive properties and to the fact that the severed lengths of the vehicle tends to adopt the shape of the sulcus after a very short time, the patient can talk, eat, smoke, drink and cough without any fear of ingesting or swallowing the vehicle.

In one particular application and embodiment the vehicles are impregnated with oxytocin, a drug which is used to induce labour in pregnancy. It will be readily appreciated that the vehicle and method described offer a further advantage, in this particular application, in that oxytocin is usually administered as an intravenous drip which is extremely inconvenient during the wait for labour to begin. The vehicle obviates the need for an intravenous drip, and can be removed as soon as the required degree of muscular contractions are evident. Thus the risk of rupturing the uterus may be substantially reduced. In this case should the vehicle be swallowed the drug will become inactivated by the stomach and no damage will advertently ensue. The vehicle also obviates some disadvantages which are inherent in compressed pulverulent tablets, e.g. such tablets are often uncomfortable and make their presence felt in the mouth and thus stimulate salivation, such salivation causing the substance to be washed away and sometimes inactivated. Therefore, the vehicle may contain a smaller dosage than a comparable tablet and yet be just as effective. Furthermore, the vehicle is absorbed in a more regular manner and "absorption peaks", and the corresponding over reactions by the patient, are avoided.

Type 2 substances, i.e. local anaesthetics, are particularly suitable for use in dentistry, and the vehicle for such use may also include antibiotics and haemostatic substances, the vehicle being superimposed upon the gum adjacent the tooth to be treated or removed, to deaden the pain of injections and the subsequent operations.

The invention is not confined to the precise details of the foregoing example and many variations are possible.

For instance an absorbable preparation may be incorporated into vehicles and administered by the method of this invention, which is particularly suitable for the administration of drugs which vary in potency according to the condition of the patient, as the vehicle may be removed when sufficient of the drug has been absorbed.

The vehicle may be prepared by any suitable means and from any suitable flexible or gelatinous material, and, in the instance wherein the material comprises mainly glycogelatine, various plasticisers and diluents may be incorporated, not only to improve and/or vary the qualities of the vehicle, but also to facilitate the production thereof, and the incorporation of the drug or drugs thereinto. Also, the vehicle may be formed, provided with a protective coating and marked linearly in a continuous operation. The vehicle may have any suitable cross-section but the cross-section should be of a size and shape commensurate with the size of the buccal sulcus of an average person. It is possible also to form smaller dimensioned vehicles suitable for treating children. Any coating provided on the vehicle may be of a type which must be removed before use, or a saliva soluble coating may be used, the vehicle being moistened with saliva before insertion into the buccal sulcus. It is also possible to embody in the vehicle a drug suitable for administration to animals.

WHAT I CLAIM IS:—

1. A vehicle for administering a drug comprising an elongate strip of resiliently flexible gelatinous material of a cross-section which enables a length thereof conveniently to be inserted into the buccal sulcus so as to adhere to the gum thereat, the vehicle containing a drug which is effective when absorbed through the buccal mucous membrane of a person, the said strip being marked or otherwise formed at intervals therealong to facilitate it being divided up to provide individual lengths or sections of desired drug content or dosage.

2. A vehicle as claimed in claim 1 wherein the drug is of a type which, if swallowed, would be destroyed or inactivated by saliva or fluids in the stomach, or would produce undesired side effects, or would require to be administered in massive overdoses.

3. A vehicle as claimed in claim 1 or 2 wherein the strip is of rectangular or square cross-section.

4. A vehicle as claimed in claim 1 or 2 wherein the strip is of oval or circular cross-section.

5. A vehicle as claimed in claim 1 or 2 wherein the strip has its two major faces respectively concave and convex.

6. A vehicle as claimed in any preceding claim wherein the strip is formed at intervals therealong with depressions extending transversely of the strip and dividing the latter into a plurality of sections each of which is connected to the next adjacent sections by readily tearable ligaments.

7. A vehicle as claimed in any of claims 1 to 5 wherein the strip is formed at intervals along one major surface thereof with ribs which divide the strip into a plurality of sections.

8. A vehicle as claimed in any preceding claim wherein the material of the vehicle is glyco-gelatine.

9. A vehicle for administering a drug substantially as hereinbefore described with reference to and as illustrated in Figs. 1 and 2, in Fig. 3, in Fig. 4, in Fig. 5, in Fig. 6, in Fig. 7, in Fig. 8, or in Fig. 10 of the accompanying drawings.

10. A vehicle as claimed in claim 1 wherein the gelatinous material of the vehicle is substantially as set forth in the foregoing example.

11. A vehicle as claimed in claim 1 wherein the drug contained therein is as hereinbefore set forth under any one of the headings Type 1 to Type 8.

12. A method of making a vehicle as claimed in any preceding claim which comprises the steps of preparing a liquid solution or melt of a gelatinous material, impregnating the solution or melt with the said drug, and then forming the said solution or melt into a vehicle by moulding or extrusion.

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Reference has been directed in pursuance of Section 9, sub-section (1) of the Patents Act, 1949, to patent Nos. 1,061,557 and 1,083,896.

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1 SHEET This drawing is a reproduction of the Original on a reduced scale

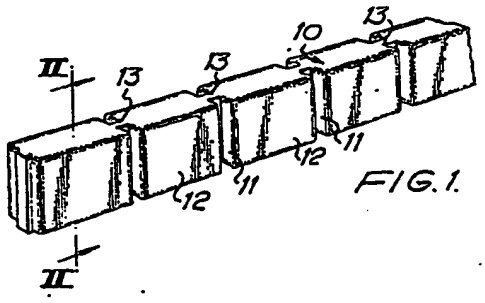

FIG. 1.

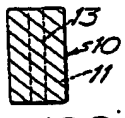

FIG. 2.

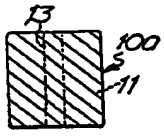

FIG. 3.

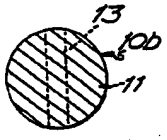

FIG. 4.

FIG. 5.

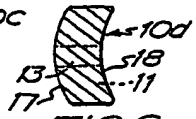

FIG. 6.

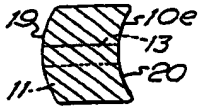

FIG. 7.

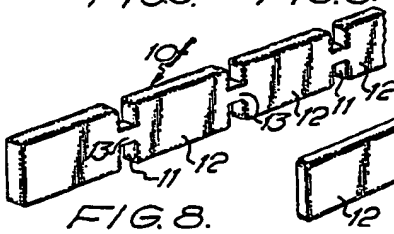

FIG. 8.

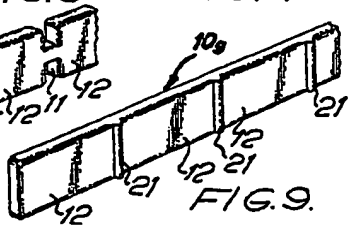

FIG. 9.

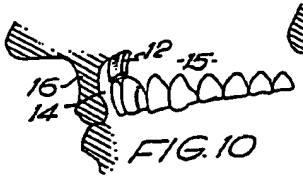

FIG. 10

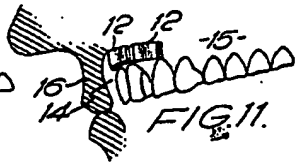

FIG. 11.